ARTICLES

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MAJOR DEPRESSION IN A LARGE FAMILY IN PAKISTAN: NO RELATIONSHIP TO INBREEDING, ECONOMIC STATUS OR RURAL LIVING

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ABSTRACT

Objective: To describe the relationships between depression and gender, socio-economic status, education, urban or rural living and coefficient of inbreeding in a well defined relatively homogeneous population.

Design: Descriptive study.

Place and Duration of Study: King Edward Medical College, Lahore from January 1999 to January 2002.

Subject and Methods: Subjects were interviewed and diagnosed by a trained psychiatrist and information was collected on various variables. Inbreeding coefficients were calculated from genealogical data.

Results: Of 211 persons interviewed, 182 had a lifetime diagnosis of recurrent major depression and 26 had no psychiatric diagnosis. Multiple regression analysis revealed greater severity and earlier age at onset in women than men but no significant correlation of severity or age at onset with socioeconomic status, urban versus rural living or coefficient of inbreeding.

Conclusion: This appears to be a genetically homogenous sub-type of depression and further genetic studies may reveal underlying genetic risk factors.

Key words: Developing countries, Psychiatric disorders, Gender, Pakistan.

INTRODUCTION

Prevalence of Major Depression varies widely between countries. In an International comparison the lifetime rates of bipolar disorder were remarkably consistent across countries but rates for major depression were less consistent ranging from 1.5% in Taiwan, 5.8% in New Zealand and 19% in Lebanon suggesting that many risk factors may be contributing1. A review of 20 published studies of the prevalence and factors associated with anxiety and depression carried out in a range of different settings in Pakistan reported an overall prevalence of depression and anxiety in the range 29%-66% for women and 10%-33% for men2. Many of the studies confirmed a greater prevalence in women and also identified social factors including low level of education, financial problems and socio-economic adversity as correlates. Mumford et al compared symptoms of a range of psychiatric illnesses including anxiety states and mild/moderate depression in two rural communities and one urban area in Pakistan3-5. The rates of moderate to severe depression in rural communities (15-33% in men and 46- 60% in women) were much higher than in the urban population where rates were 10-16% in men and 25-36% in women3. In a survey in face to face interviews with women during pregnancy in a rural district near Rawalpindi the point prevalence of depression was 25% in antenatal

women and 28% in the postnatal period but no association was found between depression and literacy level or socio-economic situation6.

Genetic factors have an important role in determining the risk of developing depression7,8. Gender differences have been consistently reported with the rate of major depression for women being about twice that of men9. There is no clear explanation for the gender effect but twin studies suggest that the heritability of depression is equal in men and women and some risk genes may have gender specific effects on phenotype10,11. Correlates identified through population surveys of depression and anxiety are difficult to interpret because it is likely that these common mental disorders are extremely heterogeneous as regards their biological and social antecedents. To develop rational interventions and treatment strategies for depression it may be essential first to identify and characterise relatively homogeneous clinical sub groups within which genetic and environmental risk factors and their interplay can be analyzed. We have adopted a different approach to studying depression in rural Pakistan by examining the relationship

between major depression and possible risk factors including years of education, socioeconomic status, urban/rural living and inbreeding by studying a single large extended family, fully ascertained from a village in rural Punjab. Single large pedigrees in genetically isolated populations offer some advantages over population cohorts for studying environmental and genetic risk factors for diseases because within families there is likely to be reduced diversity of phenotype, similarities of social and cultural factors and a reduced number of genetic risk factors. Marriages between relatives, usually cousins or second cousins, are very common within this extended family and another aim was to measure the effect of inbreeding on the severity and age at onset of depression. In offspring of first cousin marriages the risk of major birth defect is approximately doubled12 and in the Pakistani population the depression of survival between birth and age 10 in offspring of first cousin marriages is around 4% 13,14. However there is very little information on the effects of consanguinity on the incidence of common psychiatric illnesses including depression

although it has been argued, from population genetics principles, that consanguinity may contribute significantly to polygenic diseases in adulthood15. The present study is based on data from a single extended pedigree which was initially identified on account of a very high incidence of severe recurrent major depression disorder among family members whose relatedness could be accurately determined from genealogical data. The aim of this paper is to describe the relationships between depression and

gender, socio-economic status, education, urban or rural living and coefficient of inbreeding in a well defined relatively homogeneous population where the diagnosis of major depressive
disorder is based on ICD10 criteria following direct interview of all subjects by a trained psychiatrist.

SUBJECTS AND METHODS

The project had ethical approval from the appropriate ethics of research committees in Edinburgh and Lahore, informed written consent was obtained from participants who were given access to treatment if required. This large extended pedigree was ascertained by one of the authors (MA) who has known the family for about two decades since he worked as a doctor in a Rural Health Centre where many members of the family came for treatment. It was clear there was an unusual concentration of psychiatric symptoms in the family who belonged to a clan whose forebears had lived in the same agricultural area for a thousand years. There is a strong tradition of inter-marriages and villages in this region are different from those in the plains of Punjab in that they have not had an influx of population over the past two
hundred years.

Data about the pedigree were gathered through multiple interviews with family members; from genealogies kept in the villages recording male family members and from the records for the lands and their ownerships held in the Revenue Department. Sons and daughters inherit land on the death of a parent and Revenue Department records date back to the late nineteenth century. Every living descendant aged over 16 years of one founder couple identified six generations back were eligible for the study. These descendants have a preference to marry into another close branch of the family.

Clinical Diagnosis of Depression MA, a trained psychiatrist fluent in the local language, conducted interviews. Diagnoses of current and past episodes of depression were made according to ICD10 criteria and interviews were based on the Diagnostic Interview for Genetic Studies16. When a person gave a history of depression three relatives were interviewed to inquire about symptoms, prescriptions, other records of treatments and periods of hospitalization. The treating doctor was contacted for further information whenever possible. In cases where there was no evidence
of a current episode of depression in the first or subsequent interviews a diagnosis of past episodes of depression was made only if in addition to the patients description there were at least two other sources confirming the symptoms and impairment. This is a closely-knit community where information about illness including depression is openly shared and the descriptions of illness by relatives are likely to be accurate. Other relatives particularly recall hospital admission and impairment in functioning, as these are the periods when the person and their family require practical support from others. This community has frequently witnessed these episodes of recurrent major depression and clearly distinguishes depressions from general unhappiness using the name “bimari”, which literally means illness. Relatives who had
moved from the villages and were living in urban areas were traced through family links. Coefficients of inbreeding were calculated for each individual using the detailed genealogical data collected from these various sources. Over 30 English-speaking relatives were independently interviewed in English by a second psychiatrist (DB) as a measure of reliability. In no case was there a disagreement between the two raters in the diagnosis of recurrent major depression. Final diagnoses were made according to ICD10 criteria by consensus between MA and DB using all available sources of information from interviews, collateral information from relatives and hospital records. The most frequent diagnosis under ICD10 classification was recurrent depressive disorder (F33). The assessment of severity followed the ICD10 classification. We included cases that had experienced two or more episodes of depression associated with functional
impairment defined as being unable to carry out normal domestic or occupational duties and/or treatment had

Table 1:

Characteristics of depression in men and women

	Men	Women	Total	Significance
N % in group	88 (82.1)	94 (90.3)	182 (86.2)	NS
Age at Interview Mean (range)	37.4 (16-92)	38.6(16-90)	38.0(16-92)	NS
Severity of Depression				
Level of Severity	Men	Women	Total	
1	4	0	4	Chi sq=22.26 p< 0.0001
2	27	10	37	
3	50	61	111	
4	7	19	26	
5	0	4	4	

Table 2

Comparison of depressed and not depressed relatives (For socioeconomic status 1 is the lowest and 5 the highest standard of living)

	Depressed (n=182)	Not depressed (n=26)	Significance
Gender (men/women)	88/94	17/9	Chi square=2.64p=0.1
Age at interview yrs. (range)	38.0 (13-92)	32.8 (10-83)	t=1.33 (df=206)p>0.05
Education (yrs)			
0	40	2	Fishers exact test p=0.34
1-5 yrs	30	6	
5-10	85	15	
>10	27	3	
Socioeconomic status			
1	13	0	Fishers exact test p=0.34
2	58	6	
3	64	9	
4	23	6	
5	24	5	
Urban/Rural	67/115	9/17	Chi square=0.047p=0.8
3	14	1	Fisher's Exact Test P=0.448
4	70	9	
4.5	9	2	
5	88	13	
6	1	1	
Inbreeding coefficientMean (SD)	0.029 (0.034)	0.019 (0.026)	t=1.37 p=0.17

Table 3

Multivariate regression analysis of severity and age at onset of depression and some possible risk factors

	Severity of depression Beta, t and p values	Age at onset of depression Beta, t and p values
Gender	-0.241, -3, 0.003	-0.37 , 4.8, 0.000
Socioeconomic status	0.069, 0.936, 0.35	0.143, 2.02,0.045
Years of education	-0.21, -2.41, (p<0.017)	-0.521, -6.17, 0.000
Urban or rural living	0.076, 1.01, 0.312	-0.001,-0.015, 0.988
Coefficient of inbreeding	0.09, 1.25, 0.21	0.031, -0.456,0.649

DISCUSSION

Depression is a complex disorder showing marked clinical variability influenced by interacting genetic, social and cultural factors. Focusing on families and welldefined clinical sub groups may be one way to minimize aetiological heterogeneity to facilitate the discovery of genetic risk factors and clarify the relation between depression and poverty. Some types of depression may be more susceptible than others to social adversity. The sample was taken from a single settled community and was ascertained for the study when a very high incidence of recurrent depression came to the notice of doctors providing treatment at a local clinic. Once identified the whole community was surveyed avoiding
referral biases. Because this community has experienced such a high rate of depression relatives are reliable in recognizing the symptoms and this has helped them to provide good quality information to aid diagnoses. The
rate of depression did not differ across generations making it unlikely that differing attributions of illness in different generations influenced reporting especially because the gathering of clinical information involved several members of the extended family group. However a limitation of the study is the very high proportion of individuals diagnosed with depression in this family and the small number of people interviewed who had no past or present symptoms. The small sample size of the unaffected group limits the power to detect significant effects. In this community, generally one of strong religious faith where women participate in work and their roles are valued and respected, the incidence of depression was equal in women and men although with women the severity of depressive episodes was significantly greater and age at onset was younger. These findings contrast with many other studies in both high and low income
countries where the prevalence of depression has been found to be about two fold higher in women. A variety of biological, social, economic and genetic factors have been proposed to explain the gender difference including
childbirth, domestic and sexual violence and lower education levels15,18-20. However some studies which have followed cohorts with homogenous social and economic backgrounds have not found a significant difference in
rates of Major Depressive Disorder between men and women though rates of anxiety in women remain higher19.Gender effects may therefore distinguish separate sub groups of depression, a view supported by the results of some genetic linkage studies reporting sex specific loci21-23. Epidemiological studies of depression and anxiety
in several low and middle income countries worldwide have consistently reported a strong association between economic indicators including low income and poor education with common mental disorders20,24. Most surveys of mental health in rural Punjab villages have highlighted poverty, rural living and low education levels as contributing factors in depression2,3,25. In contrast this study detected no significant differences between the depressed and non-depressed group in years of education, socioeconomic status or rural living. Strikingly there was no significant correlation between socioeconomic status and severity of depression although the correlation with age at onset was weakly positive suggesting higher economic prosperity was associated with older age at onset.Although there was no difference in educational level between the depressed and the non-depressed groups, years of education showed significant inverse correlations with both severity and age at onset of depression. The inverse correlation with severity can be readily explained. Severe depression in adolescents or young adults would lead to greater drop out from school
or college hence the inverse correlation of education with severity. The inverse correlation between education and age at onset of depression reflects the presence in the clan of a group of older subjects in the village who had no education because none had been available to them and this group also reported a relatively late age at onset of symptoms. Overall these data do not support the findings from some other studies in Pakistan that increased education reduces the incidence or severity of depression.

Of relevance to this culture where marriages within the family are preferred, there was no significant correlation between coefficient of inbreeding, a measure of relatedness, and the incidence, severity or age at onset of depression. The coefficient of inbreeding in this population was very similar to that previously reported in several Indian and Pakistani populations14. The present study differed from other population surveys of depression in Pakistan villages, by its focus on one clan and in the diagnostic procedure adopted. This involved direct interview by a trained psychiatrist of all individuals participating in the study leading to a categorical diagnosis of recurrent major depression. Cases identified by these methods are likely to form a more homogeneous group than cases identified in community surveys using symptom check lists to detect common mental disorders especially if a measure of the severity of illness is not included
in the assessment20. It is likely that genetic risk factors make a substantial contribution to the high incidence of depression in this family.

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